A genomics-based method to identify cancer patients that will benefit from immune checkpoint therapy

Unmet Need

Non-small-cell lung cancer accounts for 82% of all lung cancer diagnoses. Immune checkpoint blockade treatment is an exciting new course of action among advanced stage non-small-cell lung cancer patients. However, only a minority of patients respond to immune checkpoint blockade treatment – in the U.S., the estimate percentage of patients with cancer, in general, eligible for checkpoint inhibitor drugs in 2018 was 43.63%, but less than 1% responded to the drugs. Currently, a predictor of tumor response to blockade treatment is microsatellite instability. Patients with microsatellite instability tumors were associated with better responses to blockade treatment. The field has recently discovered that a high tumor mutational burden is an even better predictor of blockade treatment response. However, given ambiguities, the suitability of tumor mutational burden for selecting patients requires additional clinical evidence. There exists an urgent need for clear identification of tumor mutations that will respond favorably to immune checkpoint blockade therapy due to the treatments' high cost and severe side effects.

Technology

Duke inventors and colleagues have developed a new genomic-based method to identify a subpopulation of non-small-cell lung cancer patients that will benefit from immune checkpoint blockade therapy. The team elucidated a mutational signature, whereby if two or more of 52 candidate genes were mutated, there would be significant immune checkpoint blockade treatment benefits in non-small-cell lung cancer patients. This ultimately defined a tumor microenvironment that is

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Publication(s)

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External Link(s)

• From the lab of Dr. Chuan-Yuan Li, D.Sc.

primed for responding to immune checkpoint blockade therapy. The compound mutation signature ensures that both a reasonably high tumor mutational burden and functionally relevant mutations are considered when selecting non-small-cell lung cancer patients for immune checkpoint blockade treatment.

Other Applications

The new genomics-based method can also be applied to other late-stage cancer treatment methods like radiotherapy and cytotoxic chemotherapy, as well as other cancer populations, such melanoma, bladder and colorectal patients, with further testing and discovery.

Advantages

- Predicts immune checkpoint blockade therapy response better than that of tumor mutational burden, capturing over 20% of patients among the four cancer types tested
- Easier patient sample collection than PD-L1 expression in non-small-cell lung cancer
- Mutations are associated with better immunotherapy outcome than tumor mutational burden status
- The method is generalized and can be applied to other cancer types with further validation